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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/583,360	06/19/2006	Runan Mei	P71315US0	3126

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JACOBSON HOLMAN PLLC
400 SEVENTH STREET N.W.
SUITE 600
WASHINGTON, DC 20004

EXAMINER

CHANDRAKUMAR, NIZAL S

ART UNIT	PAPER NUMBER
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1625

MAIL DATE	DELIVERY MODE
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10/10/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/583,360	MEI ET AL.	
	Examiner	Art Unit	
	Nizal S. Chandrakumar	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-22 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date ____ | 6) <input type="checkbox"/> Other: ____ |

DETAILED ACTION

This application filed 06/19/2006 is a 371 of PCT/CN04/01418 12/06/2004 CHINA 200310123623.X
12/19/2003 CHINA 200410044335.X 05/26/2004.

Claims 1-22 are before the Examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-22 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are generally narrative and indefinite, failing to conform to current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors.

Base claim 1 states that

the obtained crystal of
Formula I is subjected to ring closure by dehydration to
provide give-citalopram of Formula II, or citalopram is further
conversed into citalopram salts-

wherein formula I is a diol intermediate (see below).

Thus it appears that organic solid-state reactions are used for the dehydration reaction. However according to paragraph [0072] of the specification, the dehydration is performed using solution phase chemistry.

Many of the claims are redundant, restate the technical information in the same claim, and inappropriately use technical terms such as 'alkali'. The claims and specification are replete with grammatical, typographical and technical errors rendering the claims vague and indefinite.

Art Unit: 1625

1. Claim Rejections - 35 USC § 112 The following is a quotation of the first paragraph of 35 U.S.C.

112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1 and dependent claims are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to a process that involves solid-state organic chemistry. It is not seen where the specification teaches the dehydration reaction of solid crystalline diol intermediate.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 1-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over prior art.

The cyclization of purified diol (as well as resolved diol) to citalopram is taught by Bogeso et al. (US 4,650,884, column 5, Example 2).

The difference is that in the prior art, the diol intermediate is purified in solution (see column 4, Example 1) and the solution containing the diol is subjected to cyclization reaction, while in the instant case the diol is crystallized and the crystals are dissolved in a solvent and then the solution is subjected to cyclization.

The process of instant claims is drawn to purification by crystallization of the diol intermediate prior to subjecting it to cyclization reaction of Bogesso et al. Crystallization per se is a well known essential process in the practice of organic chemistry, See, Experimental Organic Chemistry, James F. Norris, Published 1924, page 3, "When an organic compound has been prepared it must be purified from the by-products which are formed at the same time. In the case of solid substances crystallization is ordinary used for this purpose....". One page 4 of this reference Norris lists the solvents that are commonly used in the crystallization processes. One skilled in the art, preparing to find methods of obtaining pure citalopram would be motivated to purify the precursor intermediate prior to subjecting it to any reaction for the preparation of citalopram, because it is well-known in the art that pure starting materials provide pure products. The instantly claimed crystallization method of Norris et al. would have been suggested.

Claim 2- 22 are drawn to purification/crystallization of diol intermediates of varying enantiomeric excesses to provide diol intermediates of varying enantiomeric excesses.

Claims 2 and 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Petersen et al. (WO 2004/056754, International filing date 12.18.2003, US priority date 12.23.2002) further in view of Bogeso et al. (US 4,650,884, column 5, Example 2).

Petersen et al. teaches the resolution of diol intermediates by precipitation to diol intermediates of various enantiomeric excesses, see pages 22-23). As indicated above Bogeso et al. (US 4,650,884, column 5, Example 2) teaches the cyclization reaction in a stereo-controlled manner.

One skilled in the art attempting to prepare optically pure S-citalopram, would be motivated to resolve the intermediate diol (purified by crystallization, see above), to optical S-diol citalopram intermediate as taught by Petersen et al. or Bogeso et al. and subject the resolved optically pure S-diol isomer to cyclization reaction.

A strong case of prima facie obviousness has been established.

Art Unit: 1625

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Li et al. (CN 15110024, STN Accession Number: 2005:519249; Document Number: 143:59681).

Li et al teach "a process for the preparation of citalopram, a drug as antidepressant, and the preparation of its intermediate I [R1 = CN, halo, alkoxy, alkylaminocarbonyl; R2 = amino containing group, amino containing aryl or cyclic ring] comprising reacting a compound of formula II with a compound of formula XCOR2 (R1, R2 are defined as above) is disclosed. For example, reaction of II (R1 = CN) with 2-chloronicotinic acid gave I (R1 = CN, R2 = 2-chloropyridin-3-yl) in 80% yield. Optical resolution of I by salification of I with di-p-toluoyl-L-tartaric acid, followed by recrystn. and hydrolysis, provided (S)-II. Cyclization of (S)-II gave optical active (S)-citalopram".

The processes of Li et al. and the processes of the instant claims are the same.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nizal S. Chandrakumar whose telephone number is 571-272-6202. The examiner can normally be reached on 8.30 am – 5 pm Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached at 571-272-0867 or Primary Examiner D. Margaret Seaman can be reached at 571-272-0694. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from

Art Unit: 1625

either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Nizal S. Chandrakumar



D. MARGARET SEAMAN
PRIMARY EXAMINER